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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/750,021	12/29/2000	Hans-Georg Frank	P66238US0	6410

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EXAMINER	
BLANCHARD, DAVID J	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 01/27/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/750,021	FRANK ET AL.	
	Examiner	Art Unit	
	David J Blanchard	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) *8-19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12/29/2000* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6/18/2001* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restrictions

1. Claims 1-19 are pending.

2. Applicant's election of Group I, now claims 1-3 and 6-7 in the paper filed 10/23/2003 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

3. The restriction requirement mailed 9/23/2003 inadvertently included claims 4 and 5 in Groups I and II. As indicated in the restriction requirement Group I is drawn to a method of making monoclonal antibodies that bind epitopes on the surface of trophoblasts or tumor cells and Group II is drawn to a method of making monoclonal antibodies that bind epitopes involved in cell-virus fusion (see below) and as such claims 4 and 5 do not read on the methods of Groups I or II. Thus, claims 4 and 5 are inclusive only to the invention of Group III as indicated below.

I. Claims 1-3 and 6-7 in part, drawn to a method of making monoclonal antibodies that bind epitopes on the surface of trophoblasts or tumor cells, classified in class 424, subclass 155.1.

II. Claims 1-3 and 6-7 in part, drawn to a method of making monoclonal antibodies that bind epitopes involved in cell-virus fusion, classified in class 424, subclass 141.1.

III. Claims 1-3 and 6-7 in part and claims 4 and 5, drawn to a method of making monoclonal antibodies that bind epitopes from endogenous antibodies, classified in class 424, subclass 152.1.

4. During a telephone conversation with William E. Player on 1/16/2004 the election of Group I, now claims 1-3 and 6-7 was maintained in view of the examiner's inadvertent inclusion of claims 4 and 5 in Groups I and II as detailed in item 3 above.

5. Claims 4-5 and 8-19 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention.

6. Claims 1-3 and 6-7 are under examination to the extent that the monoclonal immunological binding molecule is an antibody.

Specification

7. The disclosure is objected to because of the following informalities:

a. The Brief Description of the Drawings does not adequately describe figures 1 and 3. Specifically, Figures 1 and 3 have parts a and b, however, the Brief Description of the Drawings does not describe part a and part b for those figures (see page 2-3 of the specification).

b. Figure 1 is not written in English.

Appropriate correction is required.

Claim Objections

8. Claims 1 and 3 are objected to because of the following informalities:

a. Claim 1 is objected to because it is drawn to immunological binding molecules and not to an antibody.

b. Claim 3 is objected to because it is drawn to non-elected inventions. The claims are being examined to the extent that the antibody binds epitopes on the surface of trophoblasts or tumor cells.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

10. Claims 2-3 and 7 are rejected under 35 U.S.C. 112, second paragraph, as failing to set forth the subject matter which applicants regard as their invention.

a. Claims 2 and 3 are indefinite for reciting "especially single-chain antibodies" and "especially of trophoblasts or tumor cells" in claims 2 and 3, respectively. The term "especially" renders the claims indefinite because the extent or degree deserving of special emphasis in undefined. Are "single-chain antibodies" and "antibodies or antibody fragments" preferred embodiments?

b. Claim 3 is indefinite for reciting "derived" because the exact meaning of the term is not clear. The term "derived" is not one, which has a universally accepted meaning in the art nor is it one, which has been adequately defined in the specification. The primary deficiency in the use of this phrase is the absence of an ascertainable meaning for said phrase. Since it is unclear how the mammal epitopes are to be derived to yield the class of derivatives referred to in

the claim, there is no way for a person of skill in the art to ascribe a discrete and identifiable class of compounds to said phrase. In addition, since the term "derived" does not appear to be clearly defined in the specification, and the term can encompass proteins with amino acid substitutions, insertions, or deletions, chemically derivatized molecules, or even mimetics. In the absence of a single defined art recognized meaning for the phrase and lacking a definition of the term in the specification, one of skill in the art could not determine the metes and bounds of the claims.

c. Regarding claim 7, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

d. Claim 7 recites the limitation "said mammal species". There is insufficient antecedent basis for this limitation in claim 1. Claim 1 does not recite the limitation "mammal species".

e. Claim 7 is indefinite for reciting "pets" and "pests". The terms "pets" and "pests" are relative terminology and as such are indefinite because dogs, cats, mice and rats are considered "pets" in certain circumstances, yet are also considered "pests" under different circumstances. The use of the term "pets" to define dogs and cats and the term "pests" to define mice and rats are non-limiting because they are merely one interpretation of the terms. Further, the terms do not appear to be clearly defined in the specification. Thus, the metes and bounds of the claim cannot be determined.

Claim Rejections - 35 USC § 112

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claim 2 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of producing antibodies and antibody fragments that bind antigen, does not reasonably provide enablement for antibodies or antibody fragments that only have a VH or a VL chain alone and do not bind antigen as broadly encompassed by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986). They include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

The claim is broadly drawn to antibodies and antibody fragments that do not bind antigen.

The specification discloses only antibodies that contain both a VH and a VL chain and the antibodies bind antigen. The specification does not enable antibodies or antibody fragments, which only have a VH or a VL chain that do not bind antigen.

It is well established in the art that the formation of an intact antigen-binding site generally requires the association of the complete heavy and light chain variable regions of a given antibody, each of which consists of three CDRs which provide the majority of the contact residues for the binding of the antibody to its target epitope. The amino acid sequences and conformations of each of the heavy and light chain CDRs are critical in maintaining the antigen binding specificity and affinity. It is expected that all of the heavy and light chain CDRs in their proper order and in the context of framework sequences which maintain their required conformation, are required in order to produce a protein having antigen-binding function and that proper association of heavy and light chain variable regions is required in order to form functional antigen binding sites. Even minor changes in the amino acid sequences of the heavy and light variable regions, particularly in the CDRs, may dramatically affect antigen-binding function as evidenced by Rudikoff et al (Proc. Natl. Acad. Sci. USA 1982 Vol. 79 page 1979). Rudikoff et al teach that the alteration of a single amino acid in the CDR of a phosphocholine-binding myeloma protein resulted in the loss of antigen-binding function. It is unlikely that antibody fragments that only have a VH or a VL chain as defined by the claim, which would contain less than the full complement of CDRs from the heavy and light chain variable regions of an

antibody have the required binding function. The specification provides no direction or guidance regarding how to produce antibodies that only have a VH or a VL chain and bind antigen as broadly defined by the claim. Further, a fragment of the heavy chain can be any one of the constant regions (CH1-3) and also may be the hinge region. However, the language also reads on small amino acid sequences, which are incomplete regions of the constant region of the antibody. One of skill in the art would neither expect nor predict the appropriate functioning of the antibody as broadly as is claimed. Therefore, in view of the lack of guidance in the specification and in view of the discussion above one of skill in the art would be required to perform undue experimentation in order to practice the claimed invention as it pertains to.

Thus, one of skill in the art would not know how to use antibodies or antibody fragments that do not bind antigen and undue experimentation would indeed be required to produce the invention commensurate with the scope of the claims from the written disclosure alone. This rejection may be overcome by stating that the antibody fragments bind antigen.

Priority

13. Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). While the certified copy of the foreign priority document has been filed in the instant application, no certified translation has been received.

Therefore, applicants are granted the filing date of the instant application (12/29/2000).

14. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Claim Rejections - 35 USC § 102

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

16. Claims 1-3 and 7 are rejected under 35 U.S.C. 102(e) as being anticipated by Mostov et al (U.S. Patent 6,042,833, filed 6/14/1997).

Claims 1-3 and 7 recite a method of making monoclonal antibodies that bind mammal epitopes comprising (a) isolating structures containing epitopes to obtain an epitope preparation, (b) immunizing non-mammals with the epitope

preparation, (c) immortalization of the immune response to obtain a library of antibodies and (d) selection of the antibodies by means of epitope binding to obtain specific monoclonal antibodies, antibody fragments or single-chain Fv fragments (scFv) wherein the epitopes are expressed on the surfaces of cells, especially trophoblasts or tumor cells. Due to the indefinite nature of claim 7 (see 112, 2nd above), claim 7 is interpreted to mean that the mammal epitopes are selected from the group consisting of humans, dogs, cats, mice or rats.

Mostov et al teach a method of making antibodies including Fab and scFv (see column 4, lines 42-54) that bind the polymeric immunoglobulin receptor (pIgR) by immunizing chickens (see column 12-13) with pIgR and the scFvs are expressed by phage display (i.e., bacteriphage) and phage are selected using antigen (see column 8, lines 17-37 and columns 15-16). Mostov et al teach that pIgR is expressed on mammalian epithelial cells (see column 7, lines 7-10) and Mostov et al teach transfection and expression of pIgR in mammalian cells including myeloma cell lines and human colon carcinoma cells (see column 7, lines 28-34). Therefore, Mostov et al teach a method of producing antibodies that bind mammalian epitopes wherein the epitopes are expressed on tumor cells (i.e., pIgR expressed on myeloma and colon carcinoma cells).

17. Claims 1-3 and 6-7 are rejected under 35 U.S.C. 102(a) as being anticipated by Schmitz et al (Placenta. 21, Suppl. A, Trophoblast Research 14:S106-S112, 2/9/2000).

Claims 1-3 and 7 and their interpretation have been described supra (see item 16 above).

Claim 6 recites the limitation that the epitopes are oncofetal epitopes or epitopes involved in the synctial fusion of trophoblasts.

Schmitz et al teach a method of making anti-trophoblast phage display single-chain Fv (scFv) libraries by immunizing chickens with various preparations of human trophoblast cells or placental extracts (see Table 1, Figure 1 and page S108, left column). Schmitz et al teach immortalization of the immune response (see page S109, right column) and selection or panning of the antibodies using the epitope or antigen (see page S109, left column) and antigen binding Fab and scFv antibodies can be generated by phage display (see S109, right column). Schmitz et al teach that problems with immune recognition of highly conserved mammalian antigens may arise due to the phylogenetic relationship between the mouse, the usual immunological host and humans as well as other placental mammals. Because both the mouse and human placenta arise from an interstitial implantation and are haemochorial in nature, they show a comparable degree of invasiveness. Thus, a number of highly conserved trophoblast antigens will be similar in both species, resulting in reduced immunogenicity of these antigens in the mouse. Hence, species with a higher chance of recognizing these antigens can be selected for immunization including chicken, xenopus or any other suitable animal (see page S106, right column to page S108, left column).

Applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

18. Claims 1-3 and 7 are rejected under 35 U.S.C. 102(e) as being anticipated by Michael et al (U.S. Patent 6,143,559, filed 11/18/1996).

The claims and their interpretation have been described supra (see item 16 above).

Michael et al teach a method of producing monoclonal antibodies against epitopes conserved in mammalian species comprising the steps of immunizing a chicken with an antigen composition, isolation and immortalization of the B cells and selection for antigen reactivity (see column 2, lines 15-41 and column 3, lines 1-6 and columns 8-10). Michael et al teach preparing nucleic acids encoding the antigen binding regions of the light and heavy chain genes, cloning the heavy and light chain antigen binding regions in to vectors encoding the constant and leader regions, transferring the vectors into a suitable host cell, culturing the host cell and isolating the antibody (see column 3, lines 15-27). Michael et al teach that the antigen for immunization may be selected from lipids, phospholipids, carbohydrates as well as other conserved mammalian antigens (see column 3, lines 28-43) and Michael et al teach that mammals do not produce antibodies to their own proteins, making it difficult to make antibodies against certain antigenic determinants (see column 5, lines 30-39). Michael et al

teach that phage libraries have been used to generate antibodies specific for conserved antigens (see column 5, lines 40-44).

19. Claims 1-3 and 6-7 are rejected under 35 U.S.C. 102(b) as being anticipated by Hoogenboom et al (Immunotechnology. 4:1-20, 1998) as evidenced by Tendler et al (Human Pathology. 31(11):1357-1362, 2000).

The claims and their interpretation have been described supra (see item 16 above).

Hoogenboom et al teach a method of making antibody libraries wherein the antibodies are single-chain Fv fragments or Fab fragments (see page 4, left column) that bind mammalian epitopes such carcinoembryonic antigen (CEA) (see page 4, right column) as evidenced by Tendler et al. Tendler et al teach that CEA is an oncofetal glycoprotein that is overexpressed in a wide variety of tumor types (see abstract and page 1357, left column). Hoogenboom et al teach immunization of non-mammals (i.e., chickens) (see page 5, left column) and immortalization of the immune response by converting the antibodies to a form, which allows the antibodies to be produced by cells in vitro over an extended period of time (i.e., phage display). Hoogenboom et al teach a variety of selection methods by means of epitope or antigen binding (see pages 8-13 and Figures 4-5).

Claim Rejections - 35 USC § 103

20 The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

21. Claims 1-3 and 6-7 are rejected under 35 U.S.C. 103(a) as being obvious over Michael et al (U.S. Patent 6,143,559, filed 11/18/1996) in view of Schroit A.

J. (U.S. Patent 6,300,308 B1 12/31/1997) and Huppertz et al (Histochem. Cell Biol. 110:495-508, 1998, Ids 5/18/2001).

Claims 1-3 and 6-7 recite a method of making monoclonal antibodies that bind mammal epitopes comprising (a) isolating structures containing epitopes to obtain an epitope preparation, (b) immunizing non-mammals with the epitope preparation, (c) immortalization of the immune response to obtain a library of antibodies and (d) selection of the antibodies by means of epitope binding to obtain specific monoclonal antibodies wherein the epitopes are expressed on the surfaces of cells, especially trophoblasts or tumor cells or are oncofetal epitopes or epitopes involved in syncytial fusion of trophoblasts. Due to the indefinite nature of claim 7 (see 112, 2nd above), claim 7 is interpreted to mean that the mammal epitopes are selected from the group consisting of humans, dogs, cats, mice or rats.

Michael et al teach a method of producing monoclonal antibodies against epitopes conserved in mammalian species comprising the steps of immunizing a chicken or other avian species such as quails or ducks (see column 8, lines 15-18) with an antigen composition, isolation and immortalization of the B cells and selection for antigen reactivity (see column 2, lines 15-41 and column 3, lines 1-6 and columns 8-10). Michael et al teach preparing nucleic acids encoding the antigen binding regions of the light and heavy chain genes, cloning the heavy and light chain antigen binding regions in to vectors encoding the constant and leader regions, transferring the vectors into a suitable host cell, culturing the host cell and isolating the antibody (see column 3, lines 15-27). Michael et al teach

that the conserved mammalian antigens for immunization may be selected from human cystic fibrosis transmembrane conductance regulator (CFTR), transforming growth factor β, lipids, phospholipids, carbohydrates, transcription factors DNA binding molecules, cyclin dependent kinases and RNA binding proteins (see column 3, lines 28-43 and column 6, line 52-column 7, line 6 and Example 1) and Michael et al teach that mammals do not produce antibodies to their own proteins, making it difficult to make antibodies against certain antigenic determinants (see column 5, lines 30-39). Michael et al teach that phage libraries can be used to generate antibodies specific for conserved antigens (see column 5, lines 40-44). Michael et al do not specifically teach epitopes that are expressed on trophoblasts or tumor cells or oncofetal epitopes or epitopes involved in synctial fusion of trophoblasts. These deficiencies are made up for in the teachings of Schroit A. J. and Huppertz et al.

Schroit teaches a method for making phosphatidylserine specific antibodies for treating cancer (see column 2-3). Schroit teaches that membrane phospholipid asymmetry seems to be the rule for normal cells, loss of membrane lipid sidedness, in particular the emergence of phosphatidylserine (PS) at the cell surface, results in the expression of altered surface properties that modulates cell function and influences that cells interaction with its environment (see column 1, lines 29-39 and column 16, 28-33). Scroit teach "there exists a need for an effective method of producing highly-specific anti-PS antibodies and cell-mediated PS responses for use in the diagnosis and treatment of various cancers and related conditions" (see column 2, lines 36-40). Schroit teaches the

production of monoclonal antibodies by immunizing a suitable animal and the use of frog cells (i.e., non-mammal) is also possible (see column 9, lines 5-16).

Huppertz et al teach that phosphatidylserine (PS) is usually present on the inner leaflet of the plasma membrane and the appearance of PS in the outer leaflet of the plasma membrane (i.e., phosphatidylserine flip) is thought to be a signal both for cell fusion and subsequent syncytium formation (see page 495). Huppertz et al teach that phosphatidylserine flip is involved in syncytial fusion of cells and that blockade of phosphatidylserine by antibodies hinders synctium formation (see page 504, left column) and since this phosphatidylserine flip is known to be one of the earliest events in apoptosis, it suggests that apoptosis is intimately involved in trophoblast fusion and turnover (see page 495 and Figure 1).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have produced an efficient method of making antibodies that bind conserved mammalian epitopes by immunizing a non-mammal with epitopes expressed on trophoblasts, or tumor cells or oncofetal epitopes or epitopes involved in syncytial fusion of trophoblasts wherein the antibodies have diagnostic and therapeutic utility.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have produced an efficient method of making antibodies that bind conserved mammalian epitopes by immunizing a non-mammal with epitopes expressed on trophoblasts, or tumor cells or oncofetal epitopes or epitopes involved in syncytial fusion of trophoblasts

wherein the antibodies have diagnostic and therapeutic utility in view of Michael et al and Schroit A. J. and Huppertz et al because Michael et al teach method of producing monoclonal antibodies against epitopes conserved in mammalian species comprising the steps of immunizing a non-mammal (i.e., chicken) with an epitope preparation, immortalization of the immune response and selection of epitope binding antibodies and epitopes for immunization may be selected from lipids, phospholipids, carbohydrates as well as other conserved mammalian antigens and phage display can be used to generate a library of antibody molecules. In addition, one of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have produced an efficient method of making antibodies that bind conserved mammalian epitopes by immunizing a non-mammal with epitopes expressed on trophoblasts, or tumor cells or oncofetal epitopes or epitopes involved in syncytial fusion of trophoblasts wherein the antibodies have diagnostic and therapeutic utility in view of Michael et al and Schroit A. J. and Huppertz et al because Schroit A. J. teaches that in tumor cells phosphatidylserine appears at the cell surface (phosphatidylserine flip) and invokes substantial functional consequences and Huppertz et al teach that phosphatidylserine flip is involved in syncytial fusion of cells and that blockade of phosphatidylserine by antibodies hinders synctium formation and since this phosphatidylserine flip is known to be one of the earliest events in apoptosis, it suggests that apoptosis is intimately involved in trophoblast fusion and turnover. Thus, it would have been obvious to one skilled in the art to have produced an efficient method of making antibodies that bind conserved

mammalian epitopes by immunizing a non-mammal with epitopes expressed on trophoblasts, or tumor cells or oncofetal epitopes or epitopes involved in syncytial fusion of trophoblasts wherein the antibodies have diagnostic and therapeutic utility in view of Michael et al and Schroit A. J. and Huppertz et al.

Conclusion

22. No claim is allowed.

23. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Blanchard whose telephone number is (571) 272-0827. The examiner can normally be reached at (571) 272-0827 from 8:00 AM to 5:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bonnie Eyler, can be reached at (571) 272-0871. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1123.

Official papers related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The official fax number for Group 1600 where this application or proceeding is assigned is (703) 872-9306.

Respectfully,
David J. Blanchard
703-605-1200

LARRY R. HELMS, PH.D
PRIMARY EXAMINER

LARRY R. HELMS, PH.D
PRIMARY EXAMINER